REMARKS

Claims 14-26 remain in this application. Claims 23-26 are withdrawn. Claims 14-25 are currently amended.

Claims 14-25 have been amended to correct typographical errors, provide proper antecedent basis, further clarify the intended subject matter and to better conform to U.S. patent practice. No new matter has been added.

CLAIM REJECTION - 35 USC § 112

At page 2, the Office Action rejects claims 21 and 22 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The Office Action points out that claims 21 and 22 depend from cancelled claims. Currently amended claims 21 and 22 now depend from claims 20 and 21 respectively. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTION - 35 USC § 102

At page 3, the Office Action rejects claims 14-17 and 20-22 under 35 U.S.C. § 102(b) as being anticipated by CHEN et al. (Cancer Res. (1998)). Applicants respectfully traverse the rejection.

As disclosed in the specification, various constructs encoding the human/rat chimeric p185 protein have been inserted

in plasmid vectors and used in immunization experiments aimed at preventing tumor progression. Fragments of human p185neu protein containing the transmembrane domain and portions of the extracellular domain of decreasing length have been prepared from ErbB2 oncogene sequence, and portions thereof have been replaced with homologous sequences from the rat Her-2/neu cDNA so as to create chimeric plasmids. (*See,* page 4, lines 20-28, of WO 05039618).

Currently amended claim 14 is directed to a DNA transfer vector that comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, and 14. Each of the nucleotide sequences featured in claim 14 comprises a chimera of rat sequences encoding p185neu and human sequences encoding ErbB2. Such chimeric sequences are not taught or disclosed in the prior art.

Applicants elected sequence SEQ ID NO: 2 in the response to restriction requirement; thus, the Office Action has examined claims 14-22 in regard to this sequence. The Office Action holds the position that SEQ ID NO: 2 comprises rat sequences encoding p185neu but cannot further determine which portions are human and which are rat. Thus, it appears that the Office Action has essentially concluded that SEQ ID NO: 2 comprises rat sequence only. The Office Action, however, has failed to fully understand the claimed subject matter.

The specification provides full characterization of SEQ ID NO: 2 and plasmids thereof in terms of structure and biological activity. For example, the specification discloses the construction of chimeric plasmids containing the sequence of the first cysteine domain of rat p185neu, and of the second cysteine domain and transmembrane domain of human erbB2 (nt 1 to nt 1250) (*see*, page 9, line 20 to page 10, line 18, and Example 1). Continuing on, the specification discloses further plasmid constructs that encode decreasing fragments of the extracellular and transmembrane domain of human p185neu (*see*, pages 10-15). The attached Appendix includes a Figure which illustrates the composition of the claimed SEQ ID NO: 2 construct in terms of human and rat fragments, with the rat p185neu sequence defined in **bold underline** and the human sequence erbB2 sequence shown in plain text.

As discussed in the specification, the rat/human chimeric proteins encoded by the claimed nucleotide sequences are able to induce a strong humoral and cell-mediated immune response against tumors expressing oncogenes of the ErB2 family, and also provide the ability to break the "self" tolerance, thereby making the ErbB2 antigen a target for active immunization. Rat antigenic determinants present in the chimeric proteins induce a T helper response that activates B-cells and induces an antibody reaction to the "self" antigen. In addition, once the chimeric sequence is transfected and intracellularly processed, chimeric proteins are

generated that are able to tightly bind HLA molecules thereby selecting for high-affinity T cells. While the rat portion of the chimeric protein is useful to overcome the immunological tolerance to human ErbB2, the human portion provides the correct epitopes for eliciting a highly specific immune response.

Having clarified the chimeric sequence contained within SEQ ID NO: 2, it can now be stated that CHEN et al. fails to teach or suggest a DNA transfer vector comprising human erbB2 and rat p185neu coding sequences. The Office Action recognizes that CHEN is limited to the disclosure of DNA expression vectors encoding rat neu protein. CHEN absolutely fails to teach or suggest constructs of rat/human chimeric seqeunces, and fails to anticipate a DNA transfer vector comprising any of the chimeric sequences of SEQ ID NO: 1-14, as featured in present claim 14. Claims 15-17 and 20-22 depend from or otherwise include all of the limitaions of claim 14 and thus would also have not been anticipated by CHEN.

Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CLAIM REJECTION - 35 USC § 103

At page 4, the Office Action rejects claims 18-19 under 35 U.S.C. § 103(a) as being unpatentable over CHEN in view of KRIEG et al. (U.S. Patent 6,653,292). Applicants respectfully traverse the rejection.

Claims 18-19 depend from claim 14 and are directed to a DNA transfer vector comprising chimeric rat/human nucleotide sequences selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, and 14, and further comprising CpG motifs. The Office Action relies on KRIEG for the inclusion of CpG motifs in the DNA vectors.

As detailed in the above remarks, however, sequences of SEQ ID NO: 1-14 encode chimeric rat p185neu/human erbB2 sequences. CHEN and/or KRIEG, alone or in combination, fail to teach or suggest vectors comprising such chimeric rat/human nucleotide sequence.

For these reasons, CHEN and KRIEG would not have rendered obvious claims 18-19. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item:

- rat/human chimeric sequence SEQ ID NO: 2.

SEQ ID NO:2

ccgggccgga gccgcaatga tcatcatgga gctggcggcc tggtgccgct gggggttcct 60

cctcgccctc ctgccccccg gaatcgcggg cacccaagtg tgtaccggca cagacatgaa 120

gttgcggctc cctgccagtc ctgagaccca cctggacatg ctccgccacc tgtaccaggg 180

ctgtcaggta gtgcagggca acttggagct tacctacgtg cctgccaatg ccagcctctc 240

attcctgcag gacatccagg aagttcaggg ttacatgctc atcgctcaca accaggtgaa 300

gcgcgtccca ctgcaaaggc tgcgcatcgt gagagggacc cagctctttg aggacaagta 360

tgccctggct gtgctagaca accgagatcc tcaggacaat gtcgccgcct ccaccccagg 420

cagaacccca gaggggctgc gggagctgca gcttcgaagt ctcacagaga tcctgaaggg 480

aggagttttg atccgtggga accctcagct ctgctaccag gacatggttt tgtggaagga 540

cgtcttccgc aagaataacc aactggctcc tgtcgatata gacaccaatc gttcccgggc 600

ctgtccacct tgtgcccccg cctgcaaaga caatcactgt tggggtgaga gtccggaaga 660

ctgtcagatc ttgactggca ccatctgtac cagtggttgt gcccggtgca agggccggct 720

gcccactgac tgctgccatg agcagtgtgc cgcaggctgc acgggcccca agcattctga 780

ctgcctggcc tgcctccact tcaatcatag tggtatctgt gagctgcact gcccagccct 840

cgtcacctac aacacagaca cctttgagtc catgcacaac cctgagggtc gctacacctt 900

tggtgccagc tgcgtgacca cctgccccta caactacctg tctacggaag tgggatcctg 960

cactctggtg tgtcccccga ataaccaaga ggtcacagct gaggacggaa cacagcgttg 1020

tgagaaatgc agcaagccct gtgctcgagt gtgctatggt ctgggcatgg agcaccttcg 1080

aggggcgagg gccatcacca gtgacaatgt ccaggagttt gatggctgca agaagatctt 1140

tgggagcctg gcatttttgc cggagagctt tgatggggac ccctcctccg gcattgctcc 1200

gctgaggcct gagcagctcc aagtgttcga aaccctggag gagatcacag gttacctata 1260

catctcagca tggccggaca gcctgcctga cctcagcgtc ttccagaacc tgcaagtaat 1320

ccggggacga attctgcaca atggcgccta ctcgctgacc ctgcaagggc tgggcatcag 1380

ctggctgggg ctgcgctcac tgagggaact gggcagtgga ctggccctca tccaccataa 1440

cacccacctc tgcttcgtgc acacggtgcc ctgggaccag ctctttcgga acccgcacca 1500

agctctgctc cacactgcca accggccaga ggacgagtgt gtgggcgagg gcctggcctg 1560

ccaccagctg tgcgcccgag ggcactgctg gggtccaggg cccacccagt gtgtcaactg 1620

cagccagttc cttcggggcc aggagtgcgt ggaggaatgc cgagtactgc aggggctccc 1680

cagggagtat gtgaatgcca ggcactgttt gccgtgccac cctgagtgtc agccccagaa 1740

tggctcagtg acctgttttg gaccggaggc tgaccagtgt gtggcctgtg cccactataa 1800

ggaccctccc ttctgcgtgg cccgctgccc cagcggtgtg aaacctgacc tctcctacat 1860

gcccatctgg aagtttccag atgaggaggg cgcatgccag ccttgcccca tcaactgcac 1920

ccactcctgt gtggacctgg atgacaaggg ctgccccgcc gagcagagag ccagccctct 1980

gacgtccatc gtctctgcgg tggttggcat tctgctggtc gtggtcttgg gggtggtctt 2040

tgggatcctc atcaagcgac ggcagcagaa gatccggaag taa 2083

Rat neu protooncogene sequence

Human erbB2 sequence